



Review Article

Difficult endoscopic retrograde cholangiopancreatography in cancer patients

Jeffrey H. Lee*, Amanpal Singh

A B S T R A C T

Endoscopic drainage of malignant biliary obstruction can be challenging. For patients in whom conventional wire-guided cannulation or precut attempts are unsuccessful, an endoscopic ultrasound-guided approach may be helpful. Concomitant duodenal strictures occur in 10–20% of patients with malignant biliary obstruction from pancreatic cancer. Gastric outlet obstruction due to a duodenal stricture can be relieved either by endoscopic gastroduodenal stent placement or gastrojejunostomy. In this setting, simultaneous stenting of the bile duct and duodenal strictures should be considered. In this review article, we highlight the issues involved in performing endoscopic retrograde cholangiopancreatography in patients with malignancy and present a review of literature describing techniques to overcome the challenges.

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Introduction

In 1980, Laurence and Cotton¹ described two cases where duodenoscopy was used for drainage of malignant biliary strictures. Since then this procedure has gained wider acceptance than surgical or percutaneous methods. Today, endoscopic retrograde cholangiopancreatography (ERCP) is a widely used endoscopic procedure to relieve biliary obstruction caused by benign as well as malignant causes. Technical success of this procedure depends on the ability to reach and cannulate the papilla. This can be challenging in patients with underlying malignancy. In this review, we would like to highlight the various issues that relate to difficult ERCP in patients with malignancy.

Preparation for ERCP

Prior to starting a difficult ERCP, an endoscopist ought to study the patient's clinical history, indications for the procedure, and available imaging studies [computed tomography or magnetic resonance imaging (magnetic resonance cholangiopancreatography)]. Key information that can be extracted from the imaging studies includes the following:

- Patient's anatomy: Imaging studies show whether a patient has altered anatomy, such as gastric bypass, gastrojejunostomy, Billroth I or II, esophagectomy, pancreaticoduodenectomy, or

liver resection. They also demonstrate evidence of luminal (gastric, duodenal) strictures that may prevent passage of the endoscope. If the patient has gastric outlet obstruction from pancreatic or duodenal cancer, airway protection via intubation should be considered to prevent aspiration pneumonia.

- Location of the biliary stricture: If the obstruction or stricture of the bile duct is in the extrahepatic segment of the biliary tree, endotherapy to remove the cause of biliary obstruction or stenting the extrahepatic bile duct would be sufficient to re-establish bile drainage. For hilar obstruction and/or intrahepatic ductal strictures, studies comparing unilateral and bilateral stenting have yielded conflicting results. Cumulative patency durations appear to be better with bilateral stenting than with unilateral stenting, especially for patients with cholangiocarcinoma.² Occurrence of cholangitis as a procedural complication appears to be related to the injection of contrast material into a system without subsequent drainage.^{3,4} Hence, a thorough assessment of imaging studies is a requisite to plan appropriate segmental drainage of the liver for effective biliary decompression. Cannulation and contrast injection of non-drainable segments should be avoided to minimize the risk of cholangitis.

In a retrospective, two-center study, 107 patients with hilar strictures were endoscopically managed. The authors found that draining more than 50% of the liver volume was associated with

Department of Gastroenterology, Hepatology and Nutrition, University of Texas MD Anderson Cancer Center, Houston, TX, USA

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* Corresponding author. Department of Gastroenterology, Hepatology and Nutrition, University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Unit Number: 1466, Houston, TX 77030, USA.

E-mail address: jefflee@mdanderson.org (J.H. Lee).

effective drainage [odds ratio (OR) 4.5; $P = 0.001$] and a longer median survival (119 vs. 59 days; $P = 0.005$). Injection into an atrophic sector increased the risk of cholangitis (OR 3.04; $P = 0.01$).⁵ No significant difference regarding drainage success, rate of cholangitis, or survival was seen among Bismuth II, III, and IV strictures.

Finally, the endoscopist should verbally run through the procedure and cross-check the necessary accessory devices with every team member. This simple step alerts and assists the ERCP team, preventing unnecessary and midprocedural delays.

Cannulation techniques

Conventional approach

Previously published data support a higher success rate and shorter time in cannulation using a sphincterotome and a guidewire when compared with cannulation using a catheter and contrast injection. Furthermore, cannulation using a guidewire is less traumatic to the ampulla than without using one. When a tight tortuous stricture is encountered, using a short (260 cm as opposed to 450 cm) angled guidewire with a torqueing device facilitates better navigation through the narrow and tortuous biliary stricture.

Two-wire technique

Not uncommonly, selective bile duct cannulation is difficult due to the frequent inadvertent cannulation of the pancreatic duct (PD). In this case, a two-guidewire method could then be attempted. In this technique, a guidewire is inserted into the PD, and subsequent sphincterotome-assisted biliary cannulation is attempted using a second guidewire. The wire in the PD will help prevent repetitive cannulation of the PD and assist in directing the wire into the bile duct.⁶

Precut approach using a needle knife

This can be accomplished by one of the following two techniques that have similar success and complication rates:

Precut papillotomy: In this method, cutting occurs by moving the needle knife from the papillary os toward 11 or 12 o'clock position. To prevent post-ERCP pancreatitis, it is advisable to place a PD stent prior to performing precut papillotomy. This also helps orient the cutting direction toward the bile duct. In skilled hands, the complication rate of needle-knife sphincterotomy was reported not to be higher than that of the conventional pull-through sphincterotomy. Cutting should be accurately directed and sufficiently deep so as to allow biliary access, while avoiding any further unwarranted depth or misdirected cauterization.

Precut fistulotomy: In this method, free-hand cutting occurs downward from the ampullary infundibulum toward the papilla. Again, the cutting should be performed deep enough to cut into the bile duct. Most endoscopists stop cutting prior to reaching the papillary os to prevent electrocautery-induced tissue edema at the papilla resulting in post-ERCP pancreatitis.

In a prospective randomized study comparing conventional over-the-wire technique and precut approach for bile duct cannulation in 291 patients, primary precut approach was found to be as successful and safe as the conventional approach, with shorter time spent in achieving cannulation.⁷

Endoscopic ultrasound-guided ERCP

Endoscopic ultrasound (EUS)-guided biliary drainage has several variations in technique; however, all methods require

careful planning and expertise. In the EUS-guided rendezvous technique, the left hepatic duct or extrahepatic bile duct (preferably the common bile duct) is punctured with a 19-gauge needle under EUS guidance, and a guidewire is advanced down to the duodenum sequentially through the needle, stricture, and the ampulla under fluoroscopic guidance (Fig. 1). The echoendoscope is then replaced by a side-viewing scope, and the guidewire is grabbed by a snare. Once biliary access has been established, conventional ERCP can be performed. A recent study compared the efficacy of EUS-guided rendezvous technique and precut papillotomy for biliary access in difficult cannulation.⁸ The EUS-guided rendezvous technique had a significantly higher rate of technical success than that of precut papillotomy [57/58 (98.3%) vs. 130/144 (90.3%); $P = 0.03$]. Complication rates of the two techniques were similar [precut group, 6.9% and EUS group, 3.4% ($P = 0.27$)]. Precut group had one severe pancreatitis, three moderate pancreatitis, and six cases of bleeding (five mild and one moderate). EUS group had two cases of pericholedochal tracking of contrast with abdominal pain, which resolved with conservative management within 72 hours. Therefore, the EUS-guided rendezvous technique appears to offer a high technical success rate in difficult ERCP cases where conventional ERCP attempts fail.

Recently, EUS-guided biliary drainage has been described in several case series. It has applications in cases where the rendezvous procedure may not be possible because of duodenal obstruction or a difficult hilar stricture. This technique was first described in 2001.⁹ Since then, studies have described the use of EUS-guided fully covered self-expanding metal stents for patients in whom ERCP was unsuccessful due to duodenal stenosis.^{10–22} The approach can be transgastric–transhepatic or transenteric–transcholedochal, depending on the expertise of the endosonographer and the requirements of the case. In patients with previously placed biliary stents, generally a transgastric approach is favored. It involves puncturing the bile duct, confirming position by injecting a small amount of contrast and advancing a guidewire in antegrade fashion. The tract is dilated using a dilator, followed by placement of a metal stent under fluoroscopic and echoendoscopic guidance. This approach requires a good echoendoscopic assessment of the anatomy, especially in the presence of malignancy. In one report of seven patients, the authors reported failure to perform EUS-guided biliary drainage in one patient because of unfavorable anatomy.¹³ The combined placement of a duodenal stent and EUS-guided biliary drainage in patients with duodenal obstruction and biliary stricture has also been described in a case series.¹⁵

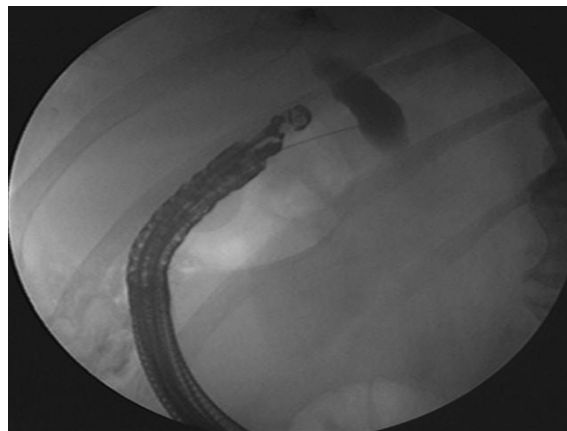


Fig. 1. Patient with pancreatic cancer presented with a duodenal stricture and obstructive jaundice. Conventional ERCP was not possible. The bile duct was accessed via EUS guidance (rendezvous). ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasound.

Thus, EUS-guided approaches offer another alternative for biliary drainage in patients with malignant obstructive jaundice. However, these techniques require an expert endosonographer and favorable anatomy. When those are not available, a good alternative with a proven track record is percutaneous trans-hepatic biliary drainage.

ERCP techniques in malignant gastric outlet obstruction

A duodenal stricture complicates biliary stent placement in 10–20% of patients with distal biliary obstruction due to pancreatic cancer. Patients with malignant gastric outlet obstruction can be palliated by endoscopic placement of a self-expanding metal stent or by gastrojejunostomy performed either open or laparoscopically. A vast body of literature has compared the outcome measures of these two palliative techniques, including procedure-related morbidity and mortality, time taken by patients in each group to tolerate oral diet, duration of hospital stay, recurrent symptoms, need for reinterventions, and cost effectiveness. Three randomized controlled studies^{23–25} and many retrospective studies have been conducted that found similar results.^{26–35} Results of some of these studies have also been summarized in systematic reviews and a meta-analysis.^{36–38} In general, the endoscopic stent placement is associated with lower morbidity and mortality, faster tolerance of oral diet, and shorter hospital stay. However, endoscopic stent placement is associated with frequent recurrence of symptoms; thus, reinterventions are often required. No significant difference in 30-day mortality was noted in the two groups. Studies comparing the costs of these two strategies found that endoscopic stent placement was associated with a lower cost.^{26,28,29,39} A recent decision analysis performed also found endoscopic stent placement to be the dominant and cost-effective strategy compared to the surgical alternative.⁴⁰ Based on the findings of these studies, endoscopic stent placement is generally considered to be the preferred procedure to relieve malignant gastric outlet obstruction.

The duodenal stricture might necessitate balloon dilation for proper duodenoscope positioning and eventual biliary stent placement. When double stenting (duodenal and biliary) is considered, biliary stenting can either precede or follow duodenal stenting (Fig. 2). Stenting of the duodenum immediately after placement of the biliary stent has the advantage of avoiding a second procedure for duodenal stenting, but lengthens the initial endoscopic procedure time. However, this is not always possible due to the duodenal strictures. Success depends on the location of the duodenal stricture in relation to the papilla. A study evaluating the feasibility of double stenting, classified duodenal strictures into three types based on the anatomical relation of duodenal stricture to the papilla⁴¹: Type I stenosis (Fig. 3), at the level of the duodenal bulb or upper duodenal genu (D1), but without involvement of the papilla; Type II stenosis, affecting the second part of the duodenum (D2), with involvement of the papilla; and Type III stenosis, involving the third part of the duodenum (D3), distal to the papilla. In patients with symptoms due to a significant duodenal stricture, a short duodenal stent can be placed without covering the ampulla, and, once the stent expands, ERCP can be attempted by passing a side-viewing scope. Extreme caution should be observed not to dislodge the duodenal stent during ERCP. When performing duodenal stenting for Type I or III duodenal stenosis, care should be taken to avoid covering the papilla. This helps preserve biliary access for any later intervention, if needed. During a combined procedure where the duodenal stent is covering the ampullary region, removal of some of the wires of the duodenal stent's mesh with rat-tooth foreign-body forceps may enable bile duct cannulation.⁴² Selective targeted melting of the mesh wires of the duodenal stent using argon plasma coagulation is another



Fig. 2. The patient had duodenal and biliary obstruction due to pancreatic cancer. Biliary obstruction developed from occlusion of a previously placed metal stent. The endoscope traversed through the duodenal stent and a plastic biliary stent was placed within the biliary metal stent.

alternative. Recently, duodenal stents with expandable lattices in the midportion to facilitate identification of the ampulla and insertion of a biliary stent have been described.⁴³ Often identifying the papilla is challenging in patients with a duodenal stricture in the second part of the duodenum (Type II stenosis). In such a patient, biliary cannulation may be easier in the presence of a previously placed biliary stent compared with a patient who has a naïve papilla (Fig. 2). Duodenal stents can help open the lumen for



Fig. 3. In this oblique view, duodenal and biliary metal stents were placed for gastric outlet obstruction and a biliary stricture.

the identification of the papilla (Fig. 3). However, this group of patients will need EUS guidance or percutaneous assistance in achieving biliary drainage.

Another technique to consider, that facilitates the passage of the duodenoscope to the papilla through the duodenal stricture, is balloon dilation (Fig. 4). In a case series published from Japan, the authors described two methods to dilate and advance the duodenoscope to reach the papilla.⁴⁴ In the first method, balloon dilation (up to a balloon diameter of 20 mm) of the stricture through the endoscope was initially performed. After the balloon was slightly deflated, the endoscope was simultaneously pushed into the distal position of the stricture (pushing method). Once the duodenal stricture was passed, the endoscope was stretched and straightened to reach the papilla. If the endoscope could not be passed through the duodenal stricture with the pushing method, in the alternative technique, the balloon was completely deflated and then advanced beyond the stricture into the third portion of the duodenum. The balloon was then reinflated and hooked at the distal position of the stricture, thereby remaining in the second or third portion of the duodenum. Finally, the endoscope was straightened, while the balloon catheter was simultaneously retracted into the working channel, allowing the endoscope to advance (hooking method). In most of these cases, after biliary cannulation and drainage, a duodenal stent was deployed to prevent restenosis of the malignant duodenal stricture. When performed, balloon dilation should be done gradually considering the severity and length of the stricture. Most importantly, when balloon dilation of the duodenal stricture is being contemplated, the endoscopist should remember that perforation and bleeding are significant risks, which can result in a major delay in the treatment of pancreatic cancer.

ERCP in surgically altered anatomy

Patients with a history of surgery for gastrointestinal cancers may subsequently develop an indication for ERCP. Patients with gastric, pancreatic, or duodenal cancers who undergo surgery either for treatment or palliation have surgically altered anatomy. In such cases, gaining access to the second portion of the duodenum is a challenge. In a study that used a large dilating balloon to gain access to the afferent limb in patients with Billroth II gastrectomy and Roux-en-Y anastomosis,⁴⁵ the authors described use of the hooking method to advance the endoscope in the afferent limb. Other techniques that have been used to accomplish endoscopic biliary drainage in patients with surgically altered anatomy include use of double balloon enteroscopy^{46–48} and laparoscopy-assisted ERCP.^{49,50} Again, perforation is a significant risk in advancing the scope through acute turns of the lumen, created by previous surgery. Thus, extreme caution should be

exercised when performing ERCP in such anatomy, keeping in mind that there is an alternative, percutaneous approach.

ERCP in patients with hematopoietic stem cell transplantation

Performing endoscopic procedures, especially therapeutic endoscopy, can be challenging in patients who have undergone hematopoietic stem cell transplantation (HSCT). These patients frequently face hepatobiliary problems due to either extension of the underlying disease or unrelated primary biliary problems. Soon after HSCT, patients develop myelosuppression resulting in pancytopenia. Pancytopenia creates several challenges for successful and safe completion of ERCP. Depending on the duration after HSCT, there is an increased risk of infections due to leukopenia. Frequently, patients develop thrombocytopenia increasing the risk of bleeding during the procedure. Further more, anemia increases the risk of cardiovascular complications related to anesthesia, due to poor reserve. Our group published ERCP experience in 40 patients who underwent the procedure after HSCT.⁵¹ The median period between HSCT and ERCP was 223 days (range 20–3805 days). The only procedural complication noted was pancreatitis. We emphasized that ERCP should only be performed in patients who would definitely benefit from the procedure in this setting, i.e., patients with imaging evidence of ductal dilation with abnormal liver enzymes, cholangitis, obstructive jaundice, and/or common bile duct stones. Another study reported the outcomes of ERCP in 16 patients who had undergone HSCT.⁵² The indication in the majority of the patients was ascending cholangitis or obstructive jaundice. There was only one complication of minor bleeding related to sphincterotomy. In this study, the average platelet count in the patients undergoing sphincterotomy was $151 \times 10^3 / \text{mm}^3$ (range $27\text{--}403 \times 10^3 / \text{mm}^3$). Regrettably, the number of patients in the study was inadequate to draw any conclusion regarding the minimum number of platelets required for safe sphincterotomy.

Cholangiopancreatography

Cholangiopancreatography (CPS) is a useful armamentarium in establishing diagnoses and providing treatments in biliary and pancreatic disorders. However, in order to be successful in CPS, one has to understand the mechanics of the instruments, procedure techniques, and, most of all, appropriate clinical applications.

One of the clinical applications of CPS is electrohydraulic lithotripsy for a large stone imbedded in the biliary tree. CPS is not necessary for ordinary biliary stone removal or visualizing a tumor with an established diagnosis. Stones located in the distal body or the tail of the PD are difficult to manage even with pancreatoscopy, especially if the duct is narrow in the head and neck of the pancreas. Hence, indications for CPS include unknown strictures in the bile duct or PD, large stones that are not retrievable by a basket or a balloon, and intraductal papillary mucinous neoplasm (to identify intraoperatively the extent of pancreatic ductal involvement). When performing CPS, sphincterotomy is necessary and the duct caliber has to be larger than the scope diameter. Gentle water irrigation is intermittently needed to optimize visualization. In performing pancreatoscopy, it is difficult to advance the scope through the genu, especially in a tortuous PD, and the scope should be advanced over the guidewire to minimize pancreatic ductal injury.⁵³ An ultraslim upper endoscope can be used for visual examination and therapeutic interventions of the bile ducts; however, this requires careful maneuvering of the scope over a guidewire placed in a branch of the intrahepatic duct, keeping in mind that excessive water irrigation without proper concurrent draining or excessive use of air can result in complications.

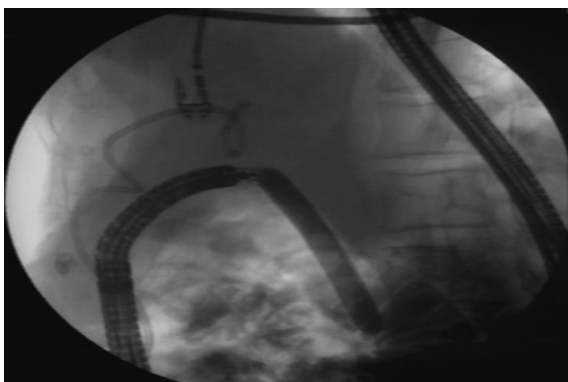


Fig. 4. Balloon dilation of stricture at the duodenal bulb (type I stenosis).

ERCP complications

ERCP complications include pancreatitis, bleeding, infection, bowel perforation, and others with the most common being pancreatitis. Pancreatitis ranges from mild to severe cases and can even result in fatal outcomes. In a large retrospective study of 11,497 ERCP procedures over 12 years, a total of 462 complications (4.0%) were reported, with 42 being severe (0.36%) and seven fatal (0.06%).⁵⁴ Pancreatitis was most common (2.6%). Overall complications were more likely among individuals with suspected sphincter of Oddi dysfunction (OR = 1.91) and following a biliary sphincterotomy (OR = 1.32). Patients with prior pancreatitis (OR = 0.78) or who received a temporary pancreatic stent (OR = 0.69) had fewer complications. Biliary sphincterotomy was associated with bleeding (OR = 4.71). Severe or fatal complications were associated with poor health status, obesity, or suspected bile duct stones, pancreatic manometry, and complex procedure. Therefore, if a patient has predictors of severe or fatal ERCP complications, perhaps preventative measures should be considered, such as observation in the hospital and/or pancreatic ductal stent placement when appropriate.

In summary, ERCPs frequently pose unique and unforeseeable challenges. Subtle changes and adjustments in techniques are often needed for successful cannulation. By far, the most important characteristics that an endoscopist should have, for safe and effective outcomes, are patience and perseverance. An endoscopy team composed of well-trained staff with experience is invaluable.

Conflict of interest

Authors have no conflict of interest.

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